IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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Applicant	:	Gerard O'Beirne	
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Examiner	:	Christian C. Boesen	
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APPEAL BRIEF

Sir:

Appellants submit this Appeal Brief, appealing from the November 17, 2009 final rejection and the June 11, 2010 Advisory Action of the Examiner, finally rejecting claims 1, 3, 4, 6, 7, 9-12 and 16-19 in the captioned application. The Notice of Appeal was filed on May 17, 2010, which contained authorization to charge the "Appeal Fee" to Appellants' Deposit Account.

Real Party in Interest

GE Healthcare UK Limited, the assignee and owner of the captioned application, is the real party in interest to this appeal.

Related Appeals and Interferences

There are no other appeals or interferences related to the instant appeal.

Status of Claims

Claims 1, 3-7, 9-13 and 16-19 are subject to examination before the U.S. Patent and Trademark Office. Claims 5 and 13 were withdrawn. Claims 1, 3, 4, 6, 7, 9-12 and 16-19 have been finally rejected and constitute the claims under appeal. A copy of the claims is appended hereto.

Status of Amendments

Appellants submit that there are no other outstanding amendments with regard to the captioned application.

Summary of Claimed Subject Matter

The instant invention relates to a novel process for determining function of one or more effector nucleic acid sequences from a library of effector nucleic acid sequences. Claim 1 is the only independent claims. Claim 1 claims the novel method for determining the function of one or more effector nucleic acid sequences from a library of effector nucleic acid sequences (lines 13-16, amended sheet 7 of the PCT application, i.e. the effector nucleic acid is equivalent of the genetic element).

In the first step, the distribution pattern of a detectable label expressed from one of a group of indicator nucleic acid sequences is determined in cells that express one of the effector nucleic acid sequences, both in the presence and the absence of one of a group of chemical modulators that affect distribution of the detectable label (see lines 14-16, page 16 of the published PCT application, where a round of screening is carried out in which effector nucleic acid sequences [10] are transfected into cells expressing the detectable fusion protein (indicator) [20] in the absence and presence

of the modulator [40]). The process is repeated with additional effector nucleic acid sequences from the library of effector nucleic acid sequences in the next step (see lines 22-27, page 16 of the PCT application).

The distribution data of the detectable label from all combinations of said effectors, modulators and indicators is analyzed to derive functional linkages among the effectors, modulators and indicators (lines 28-30, amended sheet 7 of the PCT application; see lines 10-12 and 21-26, page 18 of the PCT application). The process is repeated with different combinations of effector nucleic acid sequences, chemical modulators and indicator nucleic acid sequences until a function is assigned successfully to the one or more effector nucleic acid sequences (see lines 5-6 and 10-12, page 18 of the PCT application, i.e., "*networks of functional linkages . . . yield information on the biological function of previously uncharacterised elements*", and "*consequently yields information on the possible biological activities of the modulator and effector of the first triplet*").

Ground of Rejection to be Reviewed on Appeal

1. Whether claims 1, 3, 4, 6, 7, 9-11 and 16-19 are properly rejected under 35 U.S.C. §102(b) as being anticipated by, or under 35 U.S.C. §103(a) as being unpatentable, over Thastrup.
2. Whether claims 1, 3, 4, 6, 7, 9-12 and 16-19 are properly rejected under 35 U.S.C. §103(a) as being unpatentable over Thastrup in view of Bastiaens.
3. Whether claims 1, 3, 4, 6, 7, 9-12 and 16-19 are properly rejected under 35 U.S.C. §103(a) as being unpatentable over Thastrup in view of Bastiaens, and in view of Gonye.

Argument

1. Claims 1, 3, 4, 6, 7, 9-11 and 16-19 are not properly rejected under 35 U.S.C. §102(b) as being anticipated by, or under 35 U.S.C. §103(a) as being unpatentable, over Thastrup.

Appellants respectively submit that Thastrup is mischaracterized and do not anticipate or render obvious the claimed invention.

Appellants first submit that the specification provides definitions for key terms use in the claims. Thus, an effector is:

> *A nucleic acid sequence with biological function or activity, resulting either from an expressed protein with biological function or activity (e.g. cDNA or other coding nucleic acid sequence) or resulting from another mechanism of action (e.g. antisense and RNAi sequences).*

Lines 1-4, page 7 of the PCT application. An indicator is:

> *a nucleic acid sequence which comprises a detectable label, encodes a detectable label or which may optionally be fused to a sequence encoding a detectable protein label and expressed in a cell resulting in a characteristic localisation of the detectable protein.*

Lines 6-9, page 7. It is important to note that an indication is not simply a nucleic acid sequence which comprises a detectable label, but one that results in a characteristic localization of the detectable protein. Thus, *"[p]referably, indicator nucleic acid sequence is created by fusing the effector sequence to a nucleic acid sequence encoding a detectable label."* Paragraph bridging pages 10 and 11.

The claimed method is illustrated in Figures 3 and 4 and described in the corresponding sections of the specification. Thus, *"[t]he method of the invention may be used to establish functional relationships between genetic elements (effectors), chemical elements (modulators) and cellular assays (indicators)."* The method starts *"from collections of effectors [210] (Figure 3) and modulators [240] of known or unknown function"*. In one step, indicators are generated by engineering cDNA

effectors "*as fusions with a detectable marker protein [220]*". This is then "*transfected into target cells in the presence [270] and absence [260] of selected modulators [240]. Combinations of effectors, modulators and target cells giving a reproducible difference in the localisation of the detectable fusion protein are selected [S] for further rounds of functional screening in which the selected combinations are challenged with effectors [210] or modulators [240].*" Page 18, lines 4-14. Appellants submit that as illustrated by the definitions and the above cited sections, the fusion between a detectable marker and an effector constitutes the indicator, and the combination of indicators (i.e., effector-detectable marker fusion) and modulator in a cell is challenged by additional effectors – this is the focus of the present claim set.

The specification continues to describe the claimed invention:

> *By this means many three-way combinations of effectors, modulators and indicators may be tested [290]. Tri-partite combinations [390] (Figure 4a) in which the activity [345] of a chemical modulator [340] and the activity [315] of a genetic effector [310] on a indicator cell based assay [360] are correlated and used to infer the presence or absence of a functional linkage [301] between effector and modulator, may be used to establish functional links and clusters between many different entities. For any collections of effectors and modulators where the biological function or activity of components of the collections are both known and unknown, and where these collections are tested in combination with indicator cell assays of a known (i.e. pre-existing assays) or unknown biological significance, eight possible three-way combinations (triplets) are possible [302]-[309], and are summarised in Table 1.*

Page 18, lines 14-26. Appellants submit it is clear from the claims and the description that three elements are included in the claimed method: an indicator, a modulator, and an effector. The indicator includes a detectable label and means to render the detectable label to result in a characteristic localization. Such means may be an effector. However, Appellants assert that the claims are clear that the indicator, although may include an effector fused with a detectable label, is a separate entity

from that of the effector being assayed in step (i) of claim 1. Thus, the indicator may even include a fusion of the same effector being assayed in step (i) of claim 1, with a detectable label, as claimed in claim 9. Nonetheless, three elements are included and required for the claimed methods.

Appellants submit that Thastrup teaches using imaging to measure changes in the distribution of a luminophore, specifically GFP, within cells where the GFP is fused to a protein of known function, wherein changes in distribution of the fusion protein provides information relating to an external influence, specifically a substance having biological activity, on a cell response. Consequently Thastrup teaches a screening method for determining the activity of a substance, typically a candidate drug, against a known biological process using a GFP fusion to a DNA sequence coding for a protein of known function. However, Thastrup teaches the use of only two components;

(i) a GFP fusion protein (e.g. PKA-GFP), which is the equivalent of the indicator in the present invention; and

(ii) a test substance (e.g. forskolin), which is the equivalent of the modulator in the present invention.

The method of Thastrup provides means to determine whether a substance having biological activity is active against a chosen known cellular process, e.g. to determine if a drug candidate compound inhibits a cellular signalling pathway which is the focus of a therapeutic program. In this aspect the method of Thastrup conforms to standard drug screening methodology, i.e. providing an assay against which multiple compounds may be individually tested in parallel for activity.

Since the method of Thastrup utilizes only two components, the function of one of which by definition has to be known, the method does not teach or motivate

the method of the present invention in providing means to generate networks of functional linkages using combinations of indicators, modulators and effectors in order to assign function to an effector. No separate effector is disclosed or implied in Thastrup.

Thus, Thastrup does not anticipate or render the claims unpatentable.

2. Claims 1, 3, 4, 6, 7, 9-12 and 16-19 are not properly rejected under 35 U.S.C. §103(a) as being unpatentable over Thastrup in view of Bastiaens.

The claims 1, 3, 4, 6, 7, 9-12 and 16-19 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Thastrup in combination with Bastiaens. Appellants submit that Bastiaens does not provide any additional features which cures the deficiencies of Thastrup discussed above. Thus, Thastrup in combination with Bastiaens do not render the claims unpatentable.

3. Claims 1, 3, 4, 6, 7, 9-12 and 16-19 are not properly rejected under 35 U.S.C. §103(a) as being unpatentable over Thastrup in view of Bastiaens, and in view of Gonye.

The claims 1, 3, 4, 6, 7, 9-12 and 16-19 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Thastrup in combination with Bastiaens**, and in view of Gonye**. Appellants submit that neither Bastiaens nor Gonye provide any additional features which cures the deficiencies of Thastrup discussed above. Thus, Thastrup in combination with Bastiaens and Gonye do not render the claims unpatentable.

Conclusion

In view of the foregoing arguments, Appellants respectfully assert that the Examiner's rejections cannot be sustained and should be reversed.

Respectfully submitted,

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CLAIMS APPENDIX

The Rejected Claims

Claim 1 (previously presented): A method for determining the function of one or more effector nucleic acid sequences from a library of effector nucleic acid sequences comprising:

i) determining the distribution of a detectable label expressed from one of a group of indicator nucleic acid sequences expressed in cells in both the presence and the absence of one of a group of chemical modulators which affect said distribution of said detectable label, wherein the cells express one of said effector nucleic acid sequences;

ii) repeat step i) with a different effector nucleic acid sequence from said library of effector nucleic acid sequences;

iii) analyzing the distribution data of said detectable label from all combinations of said effectors, modulator and indicator to derive functional linkages among said effectors, modulator and indicator; and

iv) repeating steps i) to iii) with different combinations of effector nucleic acid sequences, chemical modulators and indicator nucleic acid sequences until a function is assigned successfully to said one or more effector nucleic acid sequences.

Claim 2 (cancelled)

Claim 3 (previously presented): The method of claim 1, wherein each of the effector nucleic acid sequences encodes a protein or peptide and is selected from the group

consisting of DNA, cDNA, RNA and Protein Nucleic Acid.

Claim 4 (previously presented): The method of claim 1, wherein each of the effector nucleic acid sequences is an antisense oligonucleotide.

Claim 5 (withdrawn): The method of claim 1, wherein each of the effector nucleic acid sequences is a small interfering RNA (siRNA) which causes gene silencing.

Claim 6 (previously presented): The method of claim 1, wherein each of the effector nucleic acid sequences includes a nucleic acid sequence in a cellular expression vector.

Claim 7 (original): The method of claim 6, wherein said expression vector is selected from the group consisting of plasmid, retrovirus and adenovirus.

Claim 8 (cancelled)

Claim 9 (previously presented): The method of claim 1, wherein each indicator nucleic acid sequence is created by fusing the effector nucleic acid sequence to a nucleic acid sequence encoding a detectable label.

Claim 10 (previously presented): The method of claim 1, wherein said detectable label is selected from the group consisting of fluorescent proteins, enzymes, antigens and antibodies.

Claim 11 (previously presented): The method of claim 10, wherein said fluorescent proteins are modified Green Fluorescent Proteins (GFP) having one or more mutations selected from the group consisting of Y66H, Y66W, Y66F, S65T, S65A, V68L, Q69K, Q69M, S72A, T203I, E222G, V163A, I167T, S175G, F99S, M153T, V163A, F64L, Y145F, N149K, T203Y, T203Y, T203H, S202F and L236R.

Claim 12 (previously presented): The method of claim 11, wherein said modified GFP have three mutations selected from the group consisting of F64L-V163A-E222G, F64L-S175G-E222G, F64L-S65T-S175G and F64L-S65T-V163.

Claim 13 (withdrawn): The method of claim 10, wherein said enzymes are selected from the group consisting of β-galactosidase, nitroreductase, alkaline phosphatase and β-lactamase.

Claims 14-15 (cancelled)

Claim 16 (previously presented): The method of claim 1, wherein said cells are eukaryotic cells.

Claim 17 (previously presented): The method of claim 16, wherein said eukaryotic cells are selected from the group consisting of mammal, plant, bird, fungus, fish and nematode cells, which cells may or may not be genetically modified.

Claim 18 (previously presented): The method of claim 17, wherein said mammalian cells are human cells.

Claim 19 (previously presented): The method of claim 1, wherein the distribution of the detectable label is determined using an imaging system.

Claim 20 (cancelled)

EVIDENCE APPENDIX

Appellants hereby append:

1) Thastrup et al. (WO 98/45704)
2) Bastiaens et al. (WO 2000/008054)
3) Gonye et al. (WO 01/79419)
4) Definition for Antisense downloaded from Merriam-Webster Online Dictionary 8 May 2008.

These are the evidence relied upon by the Examiner for rejection of appealed claims.

RELATED PROCEEDINGS APPENDIX

There are no other appeals or interferences related to the instant appeal.